Open Ph.D. projects

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Title of the research topic: Dissecting the mitotic role of PP2A-like protein phosphatases in fruit flies

Description of the research topic: The reproduction of cells is fundamental to the development and function of all living organisms. Therefore it must be tightly regulated and carried out with high fidelity and accuracy. The misregulation of cell division during the animal cell cycle results in serious developmental defects or cell proliferative diseases, such as cancer. Fundamental to screening for or correcting the resultant abnormalities in humans is defining their underlying molecular etiology. It is well established that besides many other postsynthetic modifications, kinase-mediated protein phosphorylation can serve as a molecular switch to fine-tune eukaryotic cell division. Key to the success of this regulatory mechanism is its reversibility; an antagonistic enzymatic activity driven by protein phosphatases. Despite this recognition, relatively little is known about how protein phosphatases govern cell division. Therefore we aim to comprehend the function of a group of PP2A-like Ser/Thr phosphatase holoenzymes that are essential to mitotic progression, but the molecular details are poorly understood. The major objective of this PhD project is the identification of phosphorylated mitotic substrates of the different PP2A-like phosphatases using AP-MS technique. Then, we will explore how dephosphorylation of the substrates contributes to cell division regulation by applying cell biological and classical genetic approaches. Finally, we wish to generate recombinant phosphatase complexes and establish dephosphorylation assays for in vitro purposes. We will utilize the Drosophila melanogaster model system, which recapitulates the phosphatase network observed in man but with the ability to integrate biochemical, cell biological, proteomic and genetic experimental approaches.